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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/660,128	09/11/2003	Avi Ashkenazi	P1245R1P2BC1	7401
9157	7590	11/13/2006	EXAMINER	
GENENTECH, INC. 1 DNA WAY SOUTH SAN FRANCISCO, CA 94080			KAUFMAN, CLAIRE M	
			ART UNIT	PAPER NUMBER
			1646	
DATE MAILED: 11/13/2006				

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/660,128

Applicant(s)

ASHKENAZI ET AL.

Examiner

Claire M. Kaufman

Art Unit

1646

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 01 September 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 38-151 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 38-151 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>12/24/03, 8/15/06</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

Applicant's election of Group III in the reply filed on 9/1/06 is acknowledged. Because Applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Even though the new composition claims 141-146 and 149 are properly grouped with Group I, they will be examined here because claims 141-146 were copied from US 7,060,272 where they appear with claims drawn to methods of inducing apoptosis.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 141-146 and 149 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 33-44, 46-54, 57 and 59-60 of copending Application No. 10/630,329 ('329) in view of US 5,763,223 (#5 in the IDS filed 12/24/03 by Applicants). The instant claims are drawn to a composition comprising an agonist antibody to DR4 and a compound that potentiates apoptosis which is TRAIL or a

Art Unit: 1646

chemotherapeutic drug. The claims of '329 are drawn to agonist antibodies that bind DR4 and induce apoptosis. TRAIL binds DR4 as admitted in the instant specification on p. 13, first sentence. US 5,763,223 teaches TRAIL and its ability to induce apoptosis in leukemia, lymphoma and melanoma cells (col. 17, lines 57-58, and col. 18, lines 6-7). It would have been obvious to combine TRAIL or a chemotherapeutic drug in a composition with the agonist DR4 antibody and since both TRAIL and chemotherapeutics were shown to be useful in the killing of cancer cells and because the binding of TRAIL to DR4 kill cells. One would have been motivated to have the composition to promote the maximum cell death in cancer cells susceptible to DR4/TRAIL-induced death.

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 147-151 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 147-151 are indefinite because they recites a “polypeptide consisting essentially of a DR4 extracellular domain”. Because the specification defines a “DR4 extracellular domain” as “essentially free of the transmembrane and cytoplasmic domains of DR4” (p. 13, line 22, emphasis added by Examiner), and the claim uses the phrase “consisting essentially of” to modify DR4 extracellular domain, it is unclear what is meant by a polypeptide consisting essentially of a region of DR4 essentially free of the transmembrane and cytoplasmic domains. The metes and bounds of the claim cannot be determined. In view of the definition in the specification, it appears that replacement of “a polypeptide consisting essentially of a” with --the--, would obviate this rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

Art Unit: 1646

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 38-51, 66-77, 90-103, 117-128 and 141-143 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to method of treating or a composition comprising an antibody that binds a polypeptide consisting of amino acids 24-238 of SEQ ID NO:1. This is not an original claim and there is no basis in the specification for the polypeptide consisting of those amino acids. The specification says the signal sequence is 1-23 and the extracellular domain ends at amino acid 218. There is nothing in the specification to lead the skilled artisan to amino acid 238 as the end of a fragment. Therefore, this is new matter.

Claims 147-151 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to an agonist antibody or fragment thereof that binds DR4 extracellular domain. The specification defines DR4 as including "native sequence DR4", which includes naturally-occurring variant forms (alternatively spliced forms) and allelic variants (p. 13, lines 6-18). The application discloses a single DR4 of SEQ ID NO:1. An agonist antibody that binds the extracellular domain of the DR4 polypeptide of SEQ ID NO:1 meets the written description provision of 35 USC 112, first paragraph. However, the claims are directed to or encompass agonist antibodies that bind polypeptides with sequences other than SEQ ID NO:1, such as corresponding sequences from other species, allelic variants and splice variants. Antibodies binding sequences other than SEQ ID NO:1 do not meet the written description provision of 35 USC 112, first paragraph.

Art Unit: 1646

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that “applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the ‘written description’ inquiry, whatever is now claimed.” (See page 1117.) The specification does not “clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed.” (See *Vas-Cath* at page 1116).

With the exception of the sequence referred to above, the skilled artisan cannot envision the detailed chemical structure of the encompassed antigen polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The nucleic acid itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF’s were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only methods or compositions in which the agonist antibody binds the extracellular domain of SEQ ID NO:1, but not the full breadth of the claims meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. § 112 is severable from its enablement provision (see page 1115).

Priority

The instant application receives an effective filing date of 1/26/98 for the pending claims.

Whenever the application has an earliest constructive reduction-to-practice that is later than the earliest constructive reduction-to-practice of a published application having allowed claims or a patent with which it interferes, the applicant must make a priority showing under 37 CFR 41.202(d)(1). The applicant may file the showing to overcome a rejection based on 35

Art Unit: 1646

U.S.C. 102(a) or 102(e) when an affidavit is not permitted under 37 CFR 1.131(a)(1) because the applicant is claiming interfering subject matter.

If no showing has been filed, and the application's earliest constructive reduction-to-practice is later than the earliest constructive reduction-to-practice of a patent or published application, then the examiner must require a showing of priority. This showing is necessary because an insufficient showing (including no showing at all) can trigger a prompt judgment against the applicant in an interference. 37 CFR 41.202(d)(2). The applicant may choose to comply with a requirement under 37 CFR 41.202(d)(1) by suggesting an interference under 37 CFR 41.202(a).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 38-151 are rejected under 35 U.S.C. 102(e) as being anticipated by US 7,060,272 (cited by Applicants in the IDS filed 8/15/06).

Applicants state in the remarks filed 9/1/06 that claims 38-146 of the instant application correspond to claims 1-29, 57-80, 105-132, 161-184 and 209-214 of the patent. Those methods and compositions claimed in the patent anticipate the methods and compositions of claims 147-151 of the instant application requiring an agonist antibody that binds the DR4 extracellular domain.

Prior Art

The prior art made of record and not relied upon is considered pertinent to Applicants' disclosure.

Art Unit: 1646

Pan et al., Science 276 :111, 4 Apr 1997, (#87 in IDS filed 12/24/03) teaches DR4 polypeptide and DR4-induced apoptosis in mammalian cells (Fig. 2). While it would have been obvious to make antibodies to this receptor or its extracellular domain, including agonist antibodies, and to use these agonist antibodies in methods of inducing apoptosis, this reference is cited only as cumulative with the reference relied upon above. The reason being that if Applicants are able to make a priority showing under 37 CFR 41.202(d)(1), then this reference will not be applicable as prior art. If Applicants are not able to make the showing, then the reference relied on with an earlier date than Pan et al. still stands as prior art.

US 6,461,823 and US 6,943,020 are cumulative with the patent relied upon above.. US 6,461,823 is the parent of which US 7,060,272 is a divisional. US 6,943,020 is a continuation of parent application 09/448,868, from which US 6,461,823 issued.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Claire M. Kaufman, whose telephone number is (571) 272-0873. Dr. Kaufman can generally be reached Monday, Tuesday, Thursday and Friday from 9:30AM to 2:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, can be reached at (571) 272-0835.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Official papers filed by fax should be directed to (571) 273-8300. NOTE: If applicant *does* submit a paper by fax, the original signed copy should be retained by the applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Art Unit: 1646

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Claire M. Kaufman, Ph.D.

A handwritten signature in black ink, appearing to read "Claire M. Kaufman", followed by a long horizontal flourish.

Patent Examiner, Art Unit 1646

November 6, 2006